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Blepharo-Cheilo-Dontic (BCD) Syndrome

Robert J. Gorlin, Hans Zellweger*, M. Waziri Curtis, Hans-Rudolf Wiedemann, Mette Warburg, Franz Majewski, Gabriele Gillessen-Kaesbach, Birte Prahl-Andersen, and Elaine Zackai

Department of Oral Sciences, University of Minnesota, Minneapolis (R.J.G.), Minnesota; Department of Pediatrics, University of Iowa, Iowa City, Iowa (H.Z.); Department of Clinical Services, Arkansas Children's Hospital, Little Rock, Arkansas (M.W.C.); Department of Pediatrics, University of Kiel, Kiel (H.-R.W.), Department of Pediatrics, Heinrich Heine University, Düsseldorf (F.M.), Institute of Human Genetics, University of Essen, Essen, Germany (G.G.-K.); Department of Ophthalmology, University of Copenhagen, Copenhagen, Denmark (M.W.); Department of Orthodontics, Vrije Universiteit, Amsterdam, The Netherlands (B.P.-A.); and Department of Pediatrics, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania (E.Z.)

Patients with the autosomal dominant blepharo-cheilo-dontic (BCD) syndrome have ectropion of lower eyelids, distichiasis of upper eyelids, euryblepharon, bilaterally cleft lip/palate, oligodontia, and conical crown form. Initially known under the eponym "Elschnig syndrome" (1912), BCD syndrome has been described in binary, ternary, and quaternary combination. There is overlap with the syndrome reported by Martínez et al. [1987], postaxial acrofacial dysostosis (Miller syndrome, Genée-Wiedemann syndrome), and a syndrome reported briefly by Warburg. © 1996 Wiley-Liss, Inc.

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INTRODUCTION

Over the past 35 years, a number of colleagues have consulted on certain cases of a facial clefting syndrome that we have chosen to categorize under a single rubric: blepharo-cheilo-dontic (BCD) syndrome. Yet, there is overlap of the eye findings of these patients with those seen in several other entities. This paper is meant to focus attention on this area and perhaps to establish a few definitions.

The first example brought to our attention is that of Piper [1957]. From reading his publication one can tell relatively little about the child he illustrated. The photograph which we used in the second edition of our text, "Syndromes of the Head and Neck," shows euryblepharon, ectropion of lower eyelids and bilaterally cleft lip/palate [Gorlin et al., 1976]. Dr. Piper concluded that the child had Elschnig syndrome. Elschnig syndrome, as defined by Leiber and Olbrich [1981], consists of (lateral) lengthening of the palpebral fissures, ectropion of the lower eyelids and lateral eye angles, variable hypertelorism, and cleft lip/palate. However, our examination of the Elschnig [1912] publication did not bolster the notion that Elschnig recognized the BCD syndrome as a distinct entity. It was recently found that the patient briefly described by Piper is Patient 3 in this publication.

Allanson and McGillivray [1985] were probably the first to report on a large, four generation family with euryblepharon, ectropion of lower eyelids, bilaterally cleft lip/palate, and anterior teeth with conical crown form. Eyebrows, eyelashes, and scalp hair were sparse. Among the 20 affected members, about 25% had cleft lip and/or palate, 40% had ectropion, and about 50% had teeth with conical crown form. Falace and Hall [1989] described a five generation kindred with euryblepharon, ectropion of the lower eyelids, teeth with conical crown form, and clefting. Among 12 affected, 4 (33%) had euryblepharon and ectropion, 2 (16%) had clefts, and 8 (75%) had abnormal teeth. Both kindreds exhibited variable expressivity of this autosomal dominant disorder. Martínez et al. [1987] described a girl with bilaterally cleft lip/palate, absence of deciduous teeth, hypodontia of permanent teeth, lagophthalmia, euryblepharon, and ectropion. The mother of the patient was reported to have a mild form of the syndrome. However, the proposita had bilateral soft tissue syndactyly of the first two fingers. The eyelashes were described as "long" and there were pili torti. Korula et al. [1995] reported on eight examples (three from one family) of a blepharo-cheilo-dontic syndrome. All had bilaterally cleft lip/palate and euryblepharon, the latter persisting as lagophthalmia. Five of the eight had disorderly eyelashes due to a double row on the upper lid. The lower lids had sparse eyelashes, especially medially. The finger- and toenails were hypoplastic in three. One had deficient teeth and one had dermoids of the lateral eyebrows.

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Address correspondence to Dr. Robert J. Gorlin, University of Minnesota School of Dentistry, 515 Delaware Street S.E., 16-127, Minneapolis, MN 55455.

*This author is deceased.

We should like to present eight cases of blepharo-cheilo-dontic (BCD) syndrome.

CLINICAL REPORTS

Patient 1

This boy was seen at the University of Iowa at 6 months for bilaterally cleft lip/palate on 6/11/74 (Fig. 1). The vomer was present. Also noted were ocular hypertelorism (inter innercanthal distance, 33 mm), ectropion, distichiasis of upper eyelids, downslanting palpebral fissures, small helix, small sinus on frontotemporal area, large umbilical hernia, and small toes. Follow-up in 1995 showed lagophthalmia. Oligodontia and microdontia were corrected by onlay dentures.

Patient 2

Mother of Patient 1 also had ocular hypertelorism. Surgery had been performed for ectropion of lower lids. Intrauterine healed bilateral cleft of upper lip was observed. She wore dentures because only 2–4 teeth ever erupted. The lacrimal puncta were not patent. Scalp hair was sparse. Radiograph of jaws showed an extremely small unerupted upper molar.

Patient 3

Patient 3 was a boy seen in the Pediatrics Department, University of Kiel, Kiel, Germany at 5 months in 1957 (Fig. 2). There was ectropion of lower eyelids, bilaterally cleft lip/palate, lagophthalmia, euryblepharon, oligodontia, and mild hypertelorism. The patient, upon investigation, was the same patient as that described very briefly by Piper [1957].

Patient 4

Patient 4 was a boy seen at age 5 years at the Institute for Human Genetics, University of Essen, Essen, Germany (Fig. 3). There were no details regarding the parents as the child was adopted. Facial anomalies included ectropion of lower lids and abundant lashes of upper eyelids. Hair, teeth, and nails were normal as was intelligence.

Fig. 2. Five-month-old boy showing ectropion of lower lids, bilateral cleft lip/palate, and euryblepharon.

Patient 5

Patient 5 was a 5-year-old girl seen at the Institute for Human Genetics, University of Düsseldorf, Düsseldorf, Germany. Noted were bilaterally cleft lip/palate, eury-

Fig. 1. Six-month-old boy with bilateral cleft lip/palate. Note ocular hypertelorism, ectropion of lower lids, and downslanting palpebral fissures.

Fig. 3. Boy exhibiting ectropion of lower eyelids, abundant upper eyelashes, sparse lower eyelashes, and euryblepharon.

blepharon, ectropion of lower eyelids, increased number of upper eyelashes, deficiency of lower eyelashes, and oligodontia with conical crown form of incisors.

Patient 6

Patient 6 was a 6-year-old boy seen at School of Dentistry, Free University, Amsterdam with bilaterally cleft lip/palate, mild hypertelorism, ectropion of lower eyelids, euryblepharon, abundant upper eyelashes, deficient lower eyelashes, somewhat sparse hair in temporal region, posterior rotation of pinnae, severe oligodontia, conical crown form of deciduous, and permanent teeth (Figs. 4, 5).

Patient 7

Patient 7 was a 2-year-old girl with sparse scalp hair, bilaterally cleft lip/palate, euryblepharon, ectropion of lower eyelids, lagophthalmia, distichiasis of upper eyelids, severe oligodontia with only one erupted conical tooth, and nasolacrimal obstruction (Fig. 6). Intelligence is normal. Height and weight are at 10–25% and head circumference below 2%.

Patient 8

The mother of Patient 7 had bilateral cleft lip and palate, lagophthalmia, oligodontia with only four molars and two deciduous teeth, and nasolacrimal obstruction. She was reported to have had a membraneous imperforate anus at birth.

DISCUSSION

The combination of signs involving the eyelids, lip, and teeth appears to be characteristic of the BCD syndrome. The upper eyelid is often the site of a double row of eyelashes (distichiasis), the lower eyelid exhibits ectropion. The palpebral fissures are wider than normal. As a result, the eyes often cannot be closed.

Fig. 5. Incisors with conical crown form.

Euryblepharon (Gr. broad lids) describes eyelids with abnormally wide lid opening. Euryblepharon is bilaterally symmetrical and is often accompanied by epiphora and conjunctivitis. Becker [1936] and Weve [1936] illustrated severe euryblepharon with ectropion of the lower lids. Duke-Elder [1963] illustrated a patient with euryblepharon, ectropion of lower lids and lagophthalmia. Ectropion of the lower eyelid may occur by itself but is also seen in postaxial acrofacial dysostosis (Miller syndrome, Genée-Wiedemann syndrome) [Opitz and Stickler, 1987; Gorlin et al., 1995].

Distichiasis refers to a congenitally formed extra row of eyelashes. The accessory row may consist of only a few cilia running along the inner part of the intermarginal strip, occupying the site of the orifices of the Meibomian glands. The lashes are usually small, soft, and fine. Distichiasis, often inherited as an isolated autosomal dominant trait [Deutsch, 1971; Mustonen, 1972], may be associated with ectropion and can be found with

Fig. 4. Boy with bilateral cleft lip/palate, euryblepharon, and ectropion of lower eyelids.

Fig. 6. Two-year-old girl showing sparse hair, bilateral cleft lip/palate, ectropion of lower eyelids, and euryblepharon.

lymphedema and/or spinal extradural cysts [Robinow et al., 1970; Shammas et al., 1979; Schwartz et al., 1980]. Picó [1957] found 13 of 20 affected in three generations with distichiasis and/or ectropion. Lagophthalmia, a condition in which the eye cannot be entirely closed, has been described in association with euryblepharon [Rodrigue, 1976]. These signs appear to distinguish the BCD syndrome from cleft lip-palate (CLP) patients with oligodontia or microdontia. Patients with CLP exhibit agenesis of teeth more often than do normal individuals. The differential diagnosis of syndromes having oligodontia and/or microdontia is legion and does not warrant discussion here. Distichiasis has been reported in combination with cleft palate in a child with Robin sequence, but there is no evidence that this child had blepharo-cheilo-dontic syndrome [Bartley and Jackson, 1989]. Neither did the patient described by Jester [1977] with lymphedema, distichiasis, and cleft palate. A male patient with some overlapping findings was seen in Gentofte Hospital, Gentofte, Denmark in 1973 by M. Warburg. Findings included repaired bilateral cleft lip/palate, euryblepharon, lagophthalmia, and ectropion of lower eyelids. However, other findings have not been found in any other patient with blepharo-cheilo-dontic syndrome. These include colobomas of choroid and optic nerve, mild microphthalmia, atrial septal defect, sensorineural hearing loss, short stature, and hypogonadism (micropenis). His appearance was illustrated in the 2nd edition of "Syndromes of the Head and Neck (1976)."

Although our Patient 4 did not have bilaterally cleft lip/palate, we have included him because the syndrome is one with variable expression as seen in the families reported by Allanson and McGillivray [1985] and Falace and Hall [1989].

CONCLUSION

The disorder which we choose to call blepharo-cheilo-dontic (BCD) syndrome is characterized by abnormalities of the a) eyelid (euryblepharon, ectropion of lower eyelids, distichiasis of upper eyelids, and lagophthalmia), b) lip (cleft lip/palate, often bilateral), and c) teeth (oligodontia, microdontia) apparently without other significant findings.

Among our eight patients with blepharo-cheilo-dontic (BCD) syndrome, there were two parent-child sets. Although expressivity of this autosomal dominant syndrome is variable, some manifestations appeared to be more common than others: ectropion of lower eyelids and, if marked, lagophthalmia. Distichiasis of the upper eyelids was a less constant finding.

Cleft lip/palate was frequent and when present was nearly always bilateral. An intrauterine healed cleft was noted in our Patient 2.

Oligodontia/microdontia was extremely variable. When present, both dentitions were affected. In one patient, there was no evidence of tooth reduction.

We propose blepharo-cheilo-dontic (BCD) syndrome as an appropriate name for the syndrome.

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